

IN THE CLAIMS

1. (original) A recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR.

2. (original) The recombinant viral vector of claim 1, wherein the termination signal sequence is the SV40 early polyadenylation signal sequence.

3. (original) The recombinant viral vector of claim 1, wherein the E2F responsive promoter is the human E2F-1 promoter.

4. (previously presented) The recombinant viral vector of claim 1, wherein the adenoviral nucleic acid backbone is derived from adenovirus serotype 5 (Ad5) or serotype 35 (Ad35).

5. (original) The recombinant viral vector of claim 1, wherein the gene essential for replication is the E1A gene.

6. (original) The recombinant viral vector of claim 1, further comprising a deletion upstream of the termination signal sequence.

7. (previously presented) The recombinant viral vector of claim 6, further comprising a deletion between nucleotides 103 and 551 of the adenoviral type 5 backbone or a deletion in nucleotides encoded by corresponding regions of other adenovirus serotypes.

8. (previously presented) The recombinant viral vector of claim 1, wherein the adenoviral nucleic acid backbone comprises an E3 region comprising a mutation or deletion.

9. (previously presented) The recombinant viral vector of claim 5, wherein the adenoviral nucleic acid backbone comprises an E4 region that is operably linked to a tissue-specific promoter.

10. (previously presented) The recombinant viral vector of claim 9, wherein said tissue-specific promoter is a human telomerase reverse transcriptase promoter.

11. (previously presented) The recombinant viral vector of claim 9, wherein said tissue-specific promoter is the Trtex promoter of SEQ ID NO:94 or the TERT promoter of SEQ ID NO:93.

12. (canceled)

13. (previously presented) The recombinant viral vector of claim 9, wherein said tissue-specific promoter is an osteocalcin promoter.

14. (previously presented) The recombinant viral vector of claim 8, wherein the E3 region has been deleted from said backbone.

15. (canceled)

16. (previously presented) The recombinant viral vector of claim 1, wherein the adenoviral nucleic acid backbone comprises an E1b gene comprising a mutation or deletion.

17. (previously presented) The recombinant viral vector of claim 16, wherein said mutation or deletion results in the loss of an active 19 kD protein expressed by the wild-type E1b gene.

18. (previously presented) The recombinant viral vector of claim 1, further comprising a coding sequence of interest.

19. (previously presented) The recombinant viral vector of claim 18, wherein said coding sequence of interest is inserted in the E3 region.

20. (previously presented) The recombinant viral vector of claim 19, wherein said coding sequence of interest is inserted in place of the 19 kD or 14.7 kD E3 gene.

21. (currently amended) The recombinant viral vector of claim 18, wherein said coding sequence of interest ~~is an~~ encodes an immunostimulatory ~~gene~~ protein.

22. (previously presented) The recombinant viral vector of claim 21, wherein said immunostimulatory protein is a cytokine.

23. (previously presented) The recombinant viral vector of claim 21, wherein the immunostimulatory protein is selected from the group consisting of GM-CSF, IL1, IL2, IL4, IL5, IFN $\alpha$ ., IFN $\gamma$ , TNF $\alpha$ , IL12, IL18, and flt3.

24. (previously presented) The recombinant viral vector of claim 21, wherein said immunostimulatory protein is selected from the group consisting of MIP1 $\alpha$ , MIP3 $\alpha$ , CCR7 ligand, calreticulin, B7, CD28, MHC class I, MHC class II, and TAPs.

25. (previously presented) The recombinant viral vector of claim 21, wherein said immunostimulatory protein is a tumor associated antigen.

26. (original) The recombinant viral vector of claim 25, wherein said tumor associated antigen is selected from the group consisting of MART-1, gp100(pmel-17), tyrosinase, tyrosinase-related protein 1, tyrosinase-related protein 2, a melanocyte-stimulating hormone receptor, MAGE1, MAGE 2, MAGE 3, MAGE 12, BAGE, GAGE, NY-ESO-1,  $\beta$ -catenin, MUM-1, CDK-4, caspase 8, KIA 0205, HLA-A2R1701,  $\alpha$ -fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic protein, p53, Her2/neu, triosephosphate isomerase, CDC-27, and LDLR-FUT.

27. (previously presented) The recombinant viral vector of claim 21, wherein said immunostimulatory protein is an antibody that blocks inhibitory signals.

28. (original) The recombinant viral vector of claim 27, wherein the inhibitory signal is due to expression of CTLA4.

29. (previously presented) The recombinant viral vector of claim 18, wherein the coding sequence of interest encodes an anti-angiogenic protein.

30. (currently amended) The recombinant viral vector of claim 29, wherein said anti-angiogenic protein is selected from the group consisting of a ~~VEGF~~VEGFR VEGF/VEGFR antagonist, an angiopoietin/Tie antagonist, an Ephrin/Eph antagonist, and an FGF/FGFR antagonist.

31. (previously presented) The recombinant viral vector of claim 29, wherein said anti-angiogenic protein is an inhibitor of PDGF, TGF $\beta$ , or IGF-1.

32. (previously presented) The recombinant viral vector of claim 29, wherein said anti-angiogenic protein is a fragment of an extracellular matrix protein.

33. (original) The recombinant viral vector of claim 32, wherein said extracellular matrix protein is selected from the group consisting of angiostatin, endostatin, kininostatin, fibrinogen-E, thrombospondin, tumstatin, canstatin, and restin.

34. (previously presented) The recombinant viral vector of claim 29, wherein the anti-angiogenic protein is a fragment of TrpRS.

35. (previously presented) The recombinant viral vector of claim 29, wherein the anti-angiogenic protein is selected from the group consisting of sFlt-1, sFlk, sNRP1, sTie-2, IP-10, PF-4, Gro-beta, IFN-gamma (Mig), sEphB4, sephrinB2, vasostatin, PEDF, prolactin fragment, proliferin-related protein, METH-1, and METH-2.

36. (previously presented) The recombinant viral vector of claim 18, wherein said coding sequence of interest encodes a protein that leads to cell death.

37. (previously presented) The recombinant viral vector of claim 36, wherein said protein that leads to cell death is selected from the group consisting of CPG2, CA, CD, cyt-450, dCK, HSV-TK, NR, PNP, TP, VZV-TK, and XGPRT.

38. (original) The recombinant viral vector of claim 1, wherein said recombinant viral vector is capable of selectively replicating in and lysing Rb-pathway defective cells.

39. (previously presented) The recombinant viral vector of claim 38, wherein replication in Rb-pathway defective cells is at least about 3-fold greater as measured by E1A RNA levels in Rb-pathway defective cells vs. non-tumor cells.

40. (original) A recombinant viral vector comprising an Ad5 nucleic acid backbone, wherein said backbone comprises in sequential order: a left ITR, an SV40 early polyA site, a human E2F-1 promoter operably linked to the E1A gene, an adenoviral packaging signal, and a right ITR.

41. (original) The recombinant viral vector of claim 40 further comprising a deletion between nucleotides 103 and 551 of the adenoviral backbone.

42. (previously presented) The recombinant viral vector of claim 40, wherein the adenoviral nucleic acid backbone comprises an E1b gene comprising a mutation or deletion, wherein said mutation or deletion results in the loss of an active 19 kD protein expressed by the wild-type E1b gene.

43. (previously presented) The recombinant viral vector of claim 40, wherein the adenoviral nucleic acid backbone comprises an E4 region that is operably linked to a tissue-specific promoter.

44. (previously presented) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is a human telomerase reverse transcriptase promoter.

45. (previously presented) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is a Trtex promoter.

46. (canceled)

47. (previously presented) The recombinant viral vector of claim 43, wherein said tissue-specific promoter is an osteocalcin promoter.

48. (currently amended) An adenoviral vector particle comprising the viral vector of ~~claims 1~~  
claim 1.

49. (original) The adenoviral vector particle of claim 48, further comprising a targeting ligand included in a capsid protein of said particle.

50. (original) The particle of claim 49, wherein said capsid protein is a fiber protein.

51. (original) The particle of claim 50, wherein said ligand is in the HI loop of said fiber protein.

52 – 57 (canceled)

58. (original) The vector of claim 1, wherein said backbone comprises a gene of the E3 coding region.

59. (original) The vector of claim 58, wherein said gene is selected from the group consisting of E3-6.7, KDa, gp19KDa, 11.6 KDa (ADP), 10.4 KDa (RID $\alpha$ ), 14.5 KDa (RID $\beta$ ), and E3-14.7Kda.

60 – 61 (canceled)

62 (previously presented) A recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises a termination signal sequence downstream of a left ITR and an E2F responsive promoter which is operably linked to a coding sequence of a gene that is essential for replication of said vector, wherein the termination signal sequence is upstream of the E2F responsive promoter; and a right ITR.

63. (previously presented) The recombinant viral vector of Claim 2, wherein the gene essential for replication is the E1A gene.

64. (previously presented) The recombinant viral vector of claim 62, wherein the termination signal sequence is an SV40 polyadenylation signal sequence.

65-66 (canceled)

67. (new) The recombinant viral vector of claim 62, wherein the adenoviral nucleic acid backbone comprises an E1b gene comprising a mutation or deletion.

68. (new) The recombinant viral vector of claim 67, wherein said mutation or deletion results in the loss of an active 19kD protein expressed by the wild-type E1b gene.

69. (new) The recombinant viral vector of claim 62, further comprising a coding sequence of interest.

70. (new) The recombinant viral vector of claim 69, wherein said coding sequence of interest

is inserted in the E3 region.

71. (new) The recombinant viral vector of claim 70, wherein said coding sequence of interest is inserted in place of the 19kD or 14.7kD E3 gene.

72. (new) The recombinant viral vector of claim 69, wherein said coding sequence of interest encodes an immunostimulatory protein.

73. (new) The recombinant viral vector of claim 72, wherein said immunostimulatory protein is a cytokine.

74. (new) The recombinant viral vector of claim 72, wherein the immunostimulatory protein is selected from the group consisting of GM-CSF, IL1, IL2, IL4, IL5, IFN.alpha., IFN.gamma., TNF.alpha., IL12, IL18, and flt3.

75. (new) The recombinant viral vector of claim 62, wherein said coding sequence of interest encodes a protein that leads to cell death.

76. (new) The recombinant viral vector of claim 62, wherein said recombinant viral vector is capable of selectively replicating in and lysing Rb-pathway defective cells.

77. (new) The recombinant viral vector of claim 76, wherein replication in Rb-pathway defective cells is at least about 3-fold as measured by E1A RNA levels in Rb-pathway defective cells vs. non-tumor cells.

78. (new) An adenoviral vector particle comprising the viral vector of claim 62.

79. (new) The adenoviral vector particle of claim 78, further comprising a targeting ligand included in a capsid protein of said particle.

80. (new) The particle of claim 79, wherein said capsid protein is a fiber protein.

81. (new) The particle of claim 79, wherein said ligand is in the HI loop of said fiber protein.

82. (new) The vector of claim 62, wherein said backbone comprises a gene of the E3 coding region.

83. (new) The vector of claim 82, wherein said gene is selected from the group consisting of E3-6.7, KDa, gp19KDa, 11.6 KDa (ADP), 10.4 KDa (RID $\alpha$ ), 14.5 KDa (RID $\beta$ ), and E3-14.7Kda.